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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,642	11/12/2003	Gloria C. Li	1747 / 55672-AA-PCT-US/JP	8975

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EXAMINER	
ZARA, JANE J	
ART UNIT	**PAPER NUMBER**
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/712,642	LI ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 10-16-06.

Claims 27-40 are pending in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejection not repeated in this Office action is hereby withdrawn.

Maintained Rejections

Claims 27-38 and 40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an in vitro method of increasing a target cell's susceptibility to DNA damaging agents comprising the administration of antisense that inhibit the expression of human Ku70, does not reasonably provide enablement for in vivo methods, and further whereby treatment has been provided in an organism for the reasons of record set forth in the Office action mailed 4-13-06.

Applicant's arguments filed 10-16-06 have been fully considered but they are not persuasive. Applicant argues that the instant invention is enabled for the full scope claimed for several reasons. Applicant argues that a working example of antisense increasing the susceptibility of a cell to DNA damaging agents has been set forth in the instant disclosure, at figure 13 and pages 12 and 83 of the specification. Contrary to

Applicant's assertions, the specification teaches an increase in radiation and chemotherapeutic sensitivity in Ku70 cells obtained from Ku70 knockout mice. This is not representative of the ability to successfully delivery adequate quantities of antisense targeting human Ku70 to an organism, whereby treatment effects are provided. The hurdle of providing adequate delivery of antisense agents to target cells in an organism is not overcome or even addressed by the experiments provided in the instant disclosure, of demonstrating a cellular phenotype in a knockout model. Applicant also argues that adenoviral mediated delivery of nucleic acids is recognized as effective, as has been illustrated by Au-Young et al (USPN 5,773,580). Applicant argues further that Crooke discusses a number of antisenses effective in vivo. Applicant is correct that Au-Young teach adenoviral vectors as suitable delivery reagents for nucleic acid expression in target cells. But, contrary to Applicant's assertions, the ability to provide treatment effects in an organism by administering antisense requires undue experimentation beyond that provided in the instant disclosure and in the art. Contrary to Applicant's assertions, the efficacy of an antisense targeting a different target gene is not predictive of the ability of a different and distinct antisense (e.g., targeting a different target gene) to provide treatment effects in a subject. The efficacy of both the antisense and an appropriate delivery device must be tested empirically, and the ability to provide treatment effects in an organism using antisense is a highly unpredictable endeavor. For these reasons, the instant rejection for lacking enablement over the scope claimed is maintained.

Claims 27, 39 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reeves et al and Milner et al, the combination in view of Taniguchi et al and Au-Young et al insofar as the claims are drawn to compositions and methods for increasing a target cell's sensitivity to DNA damaging agents in vitro comprising the administration of an antisense oligonucleotide in an adenoviral expression vector comprising a heat shock promoter, which antisense specifically hybridizes with a nucleic acid encoding a DNA dependent protein kinase subunit (Ku70), which antisense inhibits the expression of the target Ku70 subunit for the reasons of record set forth in the Office action mailed 4-13-06.

Applicant's arguments filed 10-16-06 have been fully considered but they are not persuasive. Applicant argues that the combined references do not render the instant invention obvious. Applicant argues that Au-Young teaches methods of promoting expression of a protein using an expression vector, rather than teaching a method of inhibiting expression of a protein using an adenoviral expression vector. Applicant also argues that Au-young does not teach delivery of antisense using an adenoviral expression system under the control of a heat shock promoter.

Contrary to Applicant's assertions, the combined teachings of Reeves, Milner, Taniguchi and Au-Young render the instant invention obvious. The assembly of adenoviral expression vectors was well known in the art at the time the invention was made, as well as the insertion of heat shock promoters into expression vectors, including adeno-viral vectors. The assembly of an adeno-viral expression vector comprising a heat shock promoter for driving expression of antisense in a target cell in

vitro would have required routine experimentation at the time the invention was made, and the means and motivation to do so were provided by Au-Young and many others in the art. In addition, the target gene sequence of human Ku70 was well known in the art at the time the invention was made, as taught by Reeves, and Milner taught the routine technique of designing and assessing the ability of antisense of varying lengths to inhibit the expression of a target gene of known sequence in vitro. It would have been obvious to design an adeno-viral expression vector for expression of full length antisense to human Ku70, and test its ability to inhibit the expression of human Ku70 in cells in vitro using the well known techniques taught by Au-Young and Milner, and one would have had a reasonable expectation of success in inhibiting the expression of human Ku70 using the expression constructs of the instant invention. For these reasons, the instant rejection is maintained.

Claims 27, 39 and 40 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 15, 16 and 18-22 of copending Application No. 09/750,410 for the reasons of record set forth in the Office action mailed 4-13-06.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jane Zara whose telephone number is (571) 272-0765. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz, can be reached on (571) 272-0763. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating

to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
1-6-07